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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/540,145	06/21/2005	Masatoshi Murai	44342.023000	5288

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GREENBERG TRAURIG, LLP
MET LIFE BUILDING
200 PARK AVENUE
NEW YORK, NY 10166

EXAMINER	
CHOWDHURY, IQBAL HOSSAIN	
ART UNIT	**PAPER NUMBER**
1652	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	01/30/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

TA

Office Action Summary	Application No.	Applicant(s)	
	10/540,145	MURAI, MASATOSHI	
	Examiner	Art Unit	
	Iqbal H. Chowdhury, Ph.D.	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 October 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-7 and 11-19* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7 and 11-19* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *6/05, 12/05, 7/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This application is a 371 of PCT/JP03/16653.

The preliminary amendment filed on 10/19/2006 is acknowledged. Claims 8-10 have been cancelled. Claims 1-7 and 11-19 are pending.

Applicant's election of Group I, claims 1-7 and 11-19, in the telephone conference and letter of response received by FAX on October 19, 2006 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claims 1-7 and 11-19 are under consideration and are being examined herein.

Information Disclosure Statement

The information disclosure statements (IDS) submitted on 6/21/2005, 12/19/2005 and 7/10/200611/25/2003 are acknowledged. The submission is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement is being considered by the examiner.

Drawings

The drawing of this application submitted on 6/21/2005 is being considered by the examiner.

Claim Objections

Claim1-3 and 11 are objected to; as abbreviations should not be used without at least once fully setting forth what they are used for. "PNPase" should be "polynucleotide

phosphorylase (PNPase)". Appropriate correction is required.

Claim Rejections - 35 USC § 112

New-Claim Rejections - 35 U.S.C. § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

Claim 1 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 1 recites "prokaryote-derived" which is unclear as to the scope of the polypeptide of PNPase that are encompassed. The phrase "prokaryote-derived", as it appears in the claim, is unclear as to the metes and bounds it imparts on the claimed subject matter. It is unclear whether the phrase includes only the wild type PNPase sequence or includes mutants, variants or fragments thereof, which are unknown, thereby rendering the scope of the claim(s) indefinite. The recitation "derived" can be replaced with "isolated".

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-7 and 11-19 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 1 is directed to a process for producing any PNPase, comprising constructing an expression vector comprising any PNPase gene integrated into a plasmid having a T7 promoter as an expression-regulating signal; transforming Escherichia coli or its analogous bacteria having a T7 RNA polymerase gene using the expression vector; allowing the resulting transformant to express the PNPase gene thereby accumulating PNPase in the bacteria; and recovering the bacteria having PNPase accumulated therein, and extracting and purifying the PNPase. Claim 2 recites the process further comprising a-step-of allowing the transformant to express the PNPase gene thereby accumulating PNPase in the bacteria, and further continuing to allow expression until the bacteria is disrupted to release the PNPase into a supernatant outside of the bacteria; and a-step of recovering and purifying the PNPase released in the supernatant and claim 3 recites the process, wherein the plasmid has a tag gene capable of adding a tag to the PNPase to be produced. Claim 4 recites the process, wherein the tag gene is a His tag gene, T7 tag gene, S tag gene, Nus tag gene, GST tag gene, DsbA tag gene, DsbC tag gene, CBDcex tag gene, CBDcenA tag gene, CBDclos tag gene, Trx tag gene, HSV tag gene, or 3xFLAG tag gene and claim 5 recites the process, wherein the prokaryote is Escherichia coli. Claim 6 recites the process, wherein the Escherichia coli is Escherichia coli K12 or Escherichia coli O157. Claim 7 recites the process, wherein the Escherichia coli having a T7 RNA polymerase gene is Escherichia coli BL21 [DE3], Escherichia coli 13L21 [DE3] pLysS, Escherichia coli BLR [DE3], Escherichia coli Rosetta [DE3], or Escherichia coli B834 [DE3] and claim 11 recites the process, wherein the plasmid has a tag gene capable of adding a tag to the PNPase to be produced. Claim 12 recites the process, wherein the tag gene is a His tag gene, T7 tag gene, S tag gene, Nus tag gene, GST tag gene, DsbA tag gene, DsbC tag gene, CBDcex tag gene, CBDcenA

tag gene, CBDaos tag gene, Trx tag gene, HSV tag gene, or 3xFLAG tag gene. Claim 13 recites the process, wherein the Escherichia coli having a T7 RNA polymerase gene is Escherichia coli BL21 [DE3], Escherichia coli BL21 [DE3] pLysS, Escherichia coli BLR [DE3], Escherichia coli Rosetta [DE3], or Escherichia coli B834 [DE3] and claim 14 recites the process, wherein the Escherichia coli having a T7 RNA polymerase gene is Escherichia coli BL21 [DE3], Escherichia coli BL21 [DE3] pLysS, Escherichia coli BLR [DE3], Escherichia coli Rosetta [DE3], or Escherichia coli B834 [DE3]. Claim 15 recites the process, wherein the Escherichia coli having a T7 RNA polymerase gene is Escherichia coli BL21 [DE3], Escherichia coli BL21 [DE3] pLysS, Escherichia coli BLR [DE3], Escherichia coli Rosetta [DE3], or Escherichia coli B834 [DE3] and claim 16 recites the process, wherein the Escherichia coli having a T7 RNA polymerase gene is Escherichia coli BL21 [DE3], Escherichia coli BL21 [DE3] pLysS, Escherichia coli BLR [DE3], Escherichia coli Rosetta [DE3], or Escherichia coli B834 [DE3]. Claim 17 recites the process, wherein the Escherichia coli having a T7 RNA polymerase gene is Escherichia coli BL21 [DE3], Escherichia coli BL21 [DE3] pLysS, Escherichia coli BLR [DE3], Escherichia coli Rosetta [DE3], or Escherichia coli B834 [DE3]. Claim 18 recites the process, wherein the Escherichia coli having a T7 RNA polymerase gene is Escherichia coli BL21 [DE3], Escherichia coli BL21 [DE3] pLysS, Escherichia coli BLR [DE3], Escherichia coli Rosetta [DE3], or Escherichia coli B834 [DE3] and claim 19 recites the process, wherein the Escherichia coli having a T7 RNA polymerase gene is Escherichia coli BL21 [DE3], Escherichia coli BL21 [DE3] pLysS, Escherichia coli BLR [DE3], Escherichia coli Rosetta [DE3], or Escherichia coli B834 [DE3]. As discussed in the written description guidelines the written description requirement for a claimed genus may be satisfied through sufficient

description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. A representative number of species means that the species, which are adequately described are representative of the entire genus. Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus. The specification teaches the structure of only a single representative species of such PNPase proteins.

Moreover, the specification fails to describe any other representative species by any identifying characteristics or properties other than the functionality of encoding a PNPase. Given this lack of description (i.e. structure) of representative species encompassed by the genus of DNAs used in the methods of the claim, the specification fails to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize that applicants were in possession of the claimed invention.

Claims 1-7 and 11-19 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a process for producing a PNPase encoded by the PNP gene isolated from E. coli C600K, does not reasonably provide enablement for a process for producing any PNPase protein from any source. The specification does not enable any person

skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Claim 1 is so broad as to encompass a process for producing any PNPase comprising constructing an expression vector comprising any prokaryote-derived PNPase gene including mutants, variants and recombinants of E. coli C00K PNP gene, integrated into a plasmid having a T7 promoter as an expression-regulating signal; transforming Escherichia coli or its analogous bacteria having a T7 RNA polymerase gene using the expression vector; allowing the resulting transformant to express the PNPase gene thereby accumulating PNPase in the bacteria; and recovering the bacteria having PNPase accumulated therein, and extracting and purifying the PNPase. Claim 2 recites the process further comprising a-step-of allowing the transformant to express the PNPase gene thereby accumulating PNPase in the bacteria, and further continuing to allow expression until the bacteria is disrupted to release the PNPase into a supernatant outside of the bacteria; and a-step of recovering and purifying the PNPase released in the supernatant and claim 3 recites the process, wherein the plasmid has a tag gene capable of adding a tag to the PNPase to be produced. Claim 4 recites the process, wherein the tag gene is a His tag gene, T7 tag gene, S tag gene, Nus tag gene, GST tag gene, DsbA tag gene, DsbC tag gene, CBDcex tag gene, CBDcenA tag gene, CBDclos tag gene, Trx tag gene, HSV tag gene, or 3xFLAG tag gene and claim 5 recites the process, wherein the prokaryote is Escherichia coli. Claim 6 recites the process, wherein the Escherichia coli is Escherichia coli K12 or Escherichia coli O157. Claim 7 recites the process, wherein the Escherichia coli having a T7 RNA polymerase gene is Escherichia coli BL21 [DE3], Escherichia coli 13L21 [DE3] pLysS, Escherichia coli BLR [DE3], Escherichia coli Rosetta [DE3], or Escherichia coli B834 [DE3] and claim 11 recites the

process, wherein the plasmid has a tag gene capable of adding a tag to the PNPase to be produced. Claim 12 recites the process, wherein the tag gene is a His tag gene, T7 tag gene, S tag gene, Nus tag gene, GST tag gene, DsbA tag gene, DsbC tag gene, CBDcex tag gene, CBDcenA tag gene, CBDaos tag gene, Trx tag gene, HSV tag gene, or 3xFLAG tag gene. Claim 13 recites the process, wherein the Escherichia coli having a T7 RNA polymerase gene is Escherichia coli BL21 [DE3], Escherichia coli BL21 [DE3] pLysS, Escherichia coli BLR [DE3], Escherichia coli Rosetta [DE3], or Escherichia coli B834 [DE3] and claim 14 recites the process, wherein the Escherichia coli having a T7 RNA polymerase gene is Escherichia coli BL21 [DE3], Escherichia coli BL21 [DE3] pLysS, Escherichia coli BLR [DE3], Escherichia coli Rosetta [DE3], or Escherichia coli B834 [DE3]. Claim 15 recites the process, wherein the Escherichia coli having a T7 RNA polymerase gene is Escherichia coli BL21 [DE3], Escherichia coli BL21 [DE3] pLysS, Escherichia coli BLR [DE3], Escherichia coli Rosetta [DE3], or Escherichia coli B834 [DE3] and claim 16 recites the process, wherein the Escherichia coli having a T7 RNA polymerase gene is Escherichia coli BL21 [DE3], Escherichia coli BL21 [DE3] pLysS, Escherichia coli BLR [DE3], Escherichia coli Rosetta [DE3], or Escherichia coli B834 [DE3]. Claim 17 recites the process, wherein the Escherichia coli having a T7 RNA polymerase gene is Escherichia coli BL21 [DE3], Escherichia coli BL21 [DE3] pLysS, Escherichia coli BLR [DE3], Escherichia coli Rosetta [DE3], or Escherichia coli B834 [DE3]. Claim 18 recites the process, wherein the Escherichia coli having a T7 RNA polymerase gene is Escherichia coli BL21 [DE3], Escherichia coli BL21 [DE3] pLysS, Escherichia coli BLR [DE3], Escherichia coli Rosetta [DE3], or Escherichia coli B834 [DE3] and claim 19 recites the process, wherein the Escherichia coli having a T7 RNA polymerase gene is Escherichia coli BL21 [DE3],

Escherichia coli BL21 [DE3] pLysS, Escherichia coli BLR [DE3], Escherichia coli Rosetta [DE3], or Escherichia coli B834 [DE3].

The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the method of producing extremely large number of PNPase broadly encompassed by the claims. Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function. However, in this case the disclosure is limited to the method of producing PNPase using nucleotide and encoded amino acid sequence of only one PNPase i.e. E. coli strain C600K.

While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple substitutions or multiple modifications, as encompassed by the instant claims, and the positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the result of such modifications is unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple point mutations or substitutions.

The specification does not support the broad scope of the claims which encompass a process for producing any PNPase because the specification does **not** establish: (A) regions of the protein structure which may be modified without effecting PNPase activity; (B) the general

tolerance of PNPase to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any PNPase residues with an expectation of obtaining the desired biological function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including a process for producing any PNPase. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of any PNPase to use in the claimed methods having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-4, 7 and 11-19 are rejected under 35 U.S.C. 102(b) as being anticipated by Clements et al. (Polynucleotide phosphorylase is a global regulator of virulence and persistency in Salmonella enterica, Proc Natl Acad Sci U S A. 2002 Jun 25; 99(13): 8784-9. Epub 2002 Jun 18). Clements et al. teach the process for producing Salmonella PNPase and E. coli PNPase by

constructing a vector comprising a prokaryotic PNPase encoding polynucleotide integrated in an expression vector pET30(c) having T7 promoter comprising regulatory sequence, T7 terminator having T7 tag and His Tag. Clements et al. further teach transformation of E. coli BL21 with the above vector followed by expression of PNPase protein in said E. coli as well as isolation and purification of protein according to a commercial protocol. Therefore, Clements et al. anticipates claims 1-4, 7, and 11-19 of the instant application.

Conclusion

Status of the claims:

Claims 1-7 and 11-19 are pending.

Claims 1-7 and 11-19 are rejected.

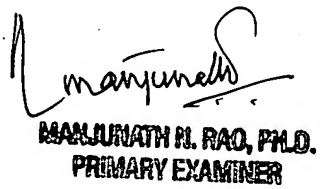
No claim is in condition for allowance.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Iqbal Chowdhury whose telephone number is 571-272-8137. The examiner can normally be reached on 9:00-5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy can be reached on 703-272-0928. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Iqbal Chowdhury, PhD, Patent Examiner
Art Unit 1652 (Recombinant Enzymes)
US Patent and Trademark Office
Rm. REM 2B69, Mail Box. 2C70
Ph. (571)-272-8137, Fax. (571)-273-8137



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